THE U.S. DEPARTMENT OF DEFENSE
PHARMACOECONOMIC CENTER

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Important Note

Over the next few months, the PEC plans to phase out hard-copy distribution of the *Update* in favor of an electronic version. If you need to continue to have a hard-copy of the *Update* mailed to you, please contact Ms. Carol Scott at the PEC:

carol.scott@amedd.army.mil

Phone: 210-295-1271
DSN 421-1271
Fax: 210-295-0323
DSN 421-0323

DoD Pharmacoeconomic Center
1750 Greeley Road
Building 4011, Room 217
Ft Sam Houston, TX 78324-6190

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Summary of Formulary Changes

Changes to the BCF

- Removal of beclomethasone and beclomethasone double-strength oral inhalers from the BCF
- Change in BCF listing for betaxolol to ophthalmic suspension as a result of the withdrawal of betaxolol ophthalmic solution

Additions to the NMOP Formulary

- pioglitazone (Actos)
- doxercalciferol (Hectorol)
- entacapone (Comtan)
- ketotifen ophthalmic solution (Zaditor)
- sermorelin (growth hormone releasing hormone) for injection (Geref)
- sirolimus solution (Rapamune)
- temozolomide (Temodar)
- zaleplon (Sonata)
- cyanocobalamin intranasal gel (Nascobal) - clarification of coverage

Other Changes to the NMOP Formulary

- Levonorgestrel tablets (Plan B; emergency contraception) - excluded from the NMOP formulary
- Rabeprazole (Aciphex) - proton pump inhibitor; listed as a "non-contracted drug" on the NMOP Formulary.

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Happy Holidays & Good Fortune in the Year 2000!

Highlights of the DoD P&T Committee Meeting

November 18, 1999
Fort Sam Houston,
Texas

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A meeting of the DoD Pharmacy & Therapeutics Committee was held 18 Nov 99 at Fort Sam Houston, Texas. The complete text of the minutes is available on the PEC website (www.pec.ha.osd.mil).

BCF Issues

Oral Inhaled Corticosteroids: The committee removed beclomethasone and beclomethasone double strength oral inhaler from the BCF due to recent price increases for Vanceril and Vanceril DS (Schering). These inhalers are now among the most costly inhalers for any given dosage range. Triamcinolone oral inhaler remains on the BCF. The committee emphasized that MTFs almost certainly need more than one oral inhaled corticosteroid on their formularies to satisfy the clinical needs of their patients, but did not want to mandate a specific inhaler by selecting another inhaler for the BCF. The committee agreed that the price instability in this drug class, along with the anticipated introduction of non-chlorofluorocarbon products and the impending introduction of a new agent, makes it difficult to ascertain which inhaler (in addition to triamcinolone) provides the greatest value. See Table 1 for a comparison of per patient per month costs for the oral inhaled corticosteroids.

Selective Serotonin Reuptake Inhibitors: The BCF currently states that MTFs must have at least one SSRI on their formularies without specifying the SSRI. The committee considered two options regarding the status of SSRIs on the BCF:

- Option 1: adding citalopram, fluoxetine, paroxetine, and sertraline to the BCF and providing information that MTFs and/or TRICARE regions could use to encourage greater use of the more cost-effective agents, or
- Option 2: continuing the current status of SSRIs on the BCF and providing information that MTFs and/or TRICARE regions could use to encourage greater use of the most cost-effective agents.

The committee selected Option 2 because of concern that Option 1 would cause large increases in expenditures for SSRIs at MTFs that currently have only one SSRI on formulary. The BCF will continue to specify that MTFs must have at least one SSRI on their formularies. The committee strongly encouraged MTFs and TRICARE regions to maximize the use of the most cost-effective SSRIs when consistent with the clinical needs of patients. More information concerning cost-effectiveness in this class will be supplied by the PEC in the near future.

Other Issues Affecting MTFs

Report of the Weight Reduction Subcommittee: TRICARE policy currently excludes coverage of drug therapy for weight reduction. Because the subcommittee's review of current drug therapies for weight reduction did not reveal a compelling clinical imperative to recommend coverage for such therapy, the committee did not recommend any change to the TRICARE policy.

Starter packs: The DOD Pharmacy Board of Directors recommended that MTFs determine local policy for the use of starter packs, with the caveat that starter packs should be dispensed by the pharmacy and not in the physician's office. Present and future contracts (and DAPAs until they are deleted) should be reviewed to ensure they incorporate language to the effect that the prices charged for the drugs shall include the cost of any starter packs which may be distributed to DoD facilities and given to patients.

Next Meeting

The next meeting of the DoD P&T Committee will be held Thursday, Feb 24, 2000

Agenda items should be submitted to the PEC no later than Friday, Jan 28, 2000

Table 1: Cost per month for oral inhaled corticosteroids (adults)

					Number of puffs per day & approximate cost per month		
NDC	Generic Name*		Puffs/ inh per unit	DAPA Price per unit (12/99)**	Low dose***	Medium dose***	High dose***
173046900	Beclomethasone (Beclovent; Glaxo) 42mcg/puff MDI 6.7 gm		80	$8.00	4 - 12 puffs $12.00 - $36.00	12 - 20 puffs $36.00 - $60.00	20 or more puffs $60.00 +
173031288	Beclomethasone (Beclovent; Glaxo) 42mcg/puff MDI 16.8 gm		200	$19.07	4 - 12 puffs $11.44 - $34.33	12 - 20 puffs $34.33- $57.21	20 or more puffs $57.21 +
85111201	Beclomethasone (Vanceril-DS; Schering) 84mcg/puff MDI		120	$28.26	2 - 6 puffs $14.13 - $42.39	6 - 10 puffs $42.39 - $70.65	10 or more puffs $70.65 +
85073604	Beclomethasone (Vanceril; Schering) 42mcg/puff MDI		200	$19.27	4 - 12 puffs $11.56 - $34.69	12 - 20 puffs $34.69- $57.81	20 or more puffs $57.81+
186091542	Budesonide (Pulmicort; Astra) 200mcg/inh DPI		200	$67.42	1 - 2 puffs $10.11 - 20.23	2 - 3 puffs $20.23 - $30.34	3 - 4 or more puffs $30.34 - 40.45 +
456067099	Flunisolide/Menthol(Aerobid-M; Forest) 250mcg/puff MDI		100	$2.79	2 - 4 puffs $1.67- $3.35	4 - 8 puffs $3.35 - $6.70	8 or more puffs $6.70 +
456067299	Flunisolide (Aerobid;Forest) 250mcg/puff MDI		100	$2.79	2 - 4 puffs $1.67- $3.35	4 - 8 puffs $3.35 - $6.70	8 or more puffs $6.70 +
173049700	Fluticasone (Flovent; Glaxo) 44mcg/puff MDI	7.9 gm	60	$19.64	2 - 6 puffs $19.64- $58.92		
173049100	Fluticasone (Flovent; Glaxo) 44mcg/puff	13 gm	120	$13.78	2 - 6 puffs $6.89 - $20.67		
173049800	Fluticasone (Flovent; Glaxo) 110mcg/puff	7.9 gm	60	$24.57	2 puffs $24.57	2 - 6 puffs $24.57 - $73.71	6 - 8 puffs $73.71- $98.28
173049400	Fluticasone (Flovent; Glaxo) 110mcg/puff	13 gm	120	$21.95	2 puffs $10.98	2 - 6 puffs $10.98 - $32.93	6 - 8 puffs $32.93 - $43.90
173049900	Fluticasone (Flovent; Glaxo) 220mcg/puff	7.9 gm	60	$38.53			3 - 4 puffs $57.80 - $77.06
173049500	Fluticasone (Flovent; Glaxo) 220mcg/puff	13 gm	120	$45.97			3 - 4 puffs $34.48 - $45.97
173051100	Fluticasone (Flovent Rotadisk; Glaxo) 50 mcg/inh DPI		60	$12.95	2 - 6 puffs $12.95 - $38.85		
173050900	Fluticasone (Flovent Rotadisk; Glaxo) 100 Mcg/Inhalation DPI		60	$14.50		3 - 6 puffs $21.75 - $43.50	6 - 10 puffs $43.50- $72.50
173050400	Fluticasone (Flovent Rotadisk; Glaxo) 250 Mcg/Inhalation DPI		60	$34.73			2 - 4 puffs $34.73- $69.46
75006037	Triamcinolone (Azmacort; RPR) 100mcg/puff MDI		240	$9.60	4 - 8 puffs $4.80 - $9.60	8 - 12 puffs $9.60 - $14.40	12 - 16 puffs $14.40 - $19.20

* MDI = metered dose inhaler; DPI = dry powder inhaler
** DAPA price for a 30-day supply as of 12/1/99 including Schering price increases effective 11/1/99
*** Dose in puffs or inhalations/day, derived from NHLBI Asthma Guidelines--Expert Panel 2 Report Figure 3-5b, page 88

HIGHLIGHTS OF THE DOD P&T COMMITTEE *Continued from Page 2*

Legislation regarding the DoD P&T Committee and DoD formulary management

The committee was briefed regarding the FY00 Defense Authorization Act, which amends Chapter 55 of title 10, United States Code, by inserting section 1074g, "Pharmacy Benefits Program." The legislation provides for the establishment of a uniform formulary, a DoD P&T Committee, and a Uniform Formulary Beneficiary Advisory Panel to review and comment on the development of the uniform formulary. [Editor's Note: text of the FY00 Defense Authorization Act may be found on the WWW at: thomas.loc.gov (search for bill "S.1059").]

Contracts: Minutes of the meeting include a complete list of DoD and DoD/VA contracts awarded to date. The committee discussed potential contracting initiatives in the following areas: estrogen replacement products, non-sedating antihistamines, and nicotine patches. Please see the complete minutes for details.

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NMOP and Retail Network

In accordance with a recent change in Chapter 7 of the TRICARE/CHAMPUS Policy Manual, quantity limits for the NMOP and retail pharmacy networks are now posted on the PEC website. The policy change also provides for the application of prior authorizations in retail network pharmacies based on the prior authorizations established for the NMOP by the DoD P&T Committee. Current lists of quantity limits and prior authorizations may be found on the PEC website under "National Mail Order Pharmacy Formulary."

NMOP Prior Authorization Forms on the Web: Due to the concerns of providers regarding the amount of time they spend dealing with phone calls and fax forms from the NMOP for drugs requiring prior authorization, prior authorization fax forms used by Merck-Medco will now be posted on the PEC website. This will give prescribers the option of filling out the form in advance and having the patient submit it to the NMOP along with the prescription. The NMOP will fill prescriptions without contacting prescribers if the correct form is submitted and if prior authorization criteria are met. The committee emphasized that the forms posted on the site are intended to facilitate sending prescriptions to the NMOP program only, not to the retail network.

Prior authorization fax forms used by Merck-Medco will now be posted on the PEC website. This will enable prescribers to fill out the form in advance and have the patient submit it to the NMOP along with the prescription.

Quantity Limits in the NMOP and Retail Network: The committee changed the 10-tablet quantity limit for zolpidem (Ambien) approved at the last meeting to the standard quantity limit of a 30-day supply for controlled substances. Pending issues include subcommittee recommendations regarding quantity limits for five high-cost topical medications, and posting on the PEC website of a complete list of all quantity limits currently in place at the NMOP (e.g., previously established quantity limits for antibiotics).

The committee also considered the quantity limit for ondansetron in light of its use for hyperemesis gravidarum by some practitioners. Consultation with MTF specialists indicated that ondansetron is not widely used or recommended for hyperemesis gravidarum. The committee decided not to change the quantity limit for ondansetron in either the NMOP or the retail network because the small number of cases where ondansetron is used for hyperemesis gravidarum can be managed on an exception basis. Ondansetron is Pregnancy Category B and should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Prior Authorization for Oral Antifungal Medications (NMOP and Retail Network): TMA officials asked the committee to render an opinion about prior authorization criteria that attempt to differentiate between cosmetic and non-cosmetic use of oral terbinafine (Lamisil; Novartis) for onychomycosis. The committee reached general agreement on the following points:

- It is difficult to clearly define and accurately differentiate cosmetic and non-cosmetic use of terbinafine.
- Systemic antifungal therapy should not be instituted unless the presence of a fungal infection is clearly established by KOH prep, culture, or PAS stain. Use of systemic antifungal therapy in the absence of a fungal infection unnecessarily exposes the patient to the risk of adverse effects and wastes money.
- Pulse dosing of terbinafine for the treatment of onychomycosis appears to be effective for onychomycosis and offers an economic advantage over daily dosing.
- Even though the initial treatment with oral terbinafine usually eliminates the fungal infection, the nails may remain discolored until they grow out. It is inappropriate to continue oral terbinafine therapy just because the nails are discolored.
- A prior authorization program for oral terbinafine could potentially shift usage to itraconazole, which is even more expensive than terbinafine for onychomycosis.

The committee concluded that oral terbinafine should be subject to prior authorization that focuses on the appropriate diagnosis of onychomycosis and appropriate duration of therapy. Committee co-chairs will finalize the prior authorization criteria for oral terbinafine. The prior authorization program for oral terbinafine will be monitored for a shift in usage to the more expensive agent.

Prior Authorization for Growth Hormone Treatment: In light of the costs associated with growth hormone treatment and the potential for inappropriate use, a subcommittee was appointed to evaluate current utilization in the NMOP and retail networks, recommend prior authorization criteria, and estimate potential cost savings associated with a prior authorization program.

NMOP

Please see the summary on Page 1 and the complete text of the minutes for changes to the NMOP Formulary.

Cost-Effective Treatment for Onychomycosis

Until recently, onychomycosis was viewed as a relatively incurable condition. This is due in part to the ineffectiveness of previously available therapy, poor compliance with prolonged regimens (e.g., griseofulvin) and low visibility of this largely cosmetic condition to the public. With the availability of newer oral antifungal drugs, the medical community has more effective and better tolerated oral agents for the treatment of onychomycosis.

Terbinafine (Lamisil®; Novartis) is an orally active, allylamine (non-azole) antifungal agent indicated for onychomycosis. As a continuous regimen, the dosage of terbinafine is 250 mg po QD for 6 weeks for fingernails and 12 weeks for toenails. Treatment should not be repeated for 3-6 months in order to allow the diseased nail to grow out and be replaced by new, healthy, uninfected nailplate. Liver function tests and complete blood counts should be taken at baseline and again at 6 weeks of terbinafine therapy for evidence of liver toxicity and/or neutropenia. Although generally well tolerated, there have been isolated cases of toxic epidermal necrolysis, Stevens-Johnson Syndrome, and cholestatic hepatitis in patients treated with terbinafine.

Terbinafine reaches therapeutic levels in the nailplate after 24-48 hours, then forms a reservoir of drug that remains in the nailplate for at least 2-3 weeks after therapy is stopped. Pulse dosing with terbinafine is therefore mechanistically plausible. The Brooke Army Medical Center Dermatology Department advocates pulse dosing of terbinafine for onychomycosis because pulse dosing requires only half as much drug and, based on their clinical experience, appears to be similar to continuous dosing in effectiveness. Continuous and pulse dosing regimens of terbinafine for onychomycosis have not been compared in large clinical trials. In a small randomized trial, Tosti *et al* reported the following mycological cure rates at 6 months after completion of 12 weeks of treatment for toenail onychomycosis: 94% (16 of 17 patients) with continuous terbinafine; 80% (16/20) with pulse terbinafine; and 75% (15/20) with pulse itraconazole. The differences in cure rates were not statistically significant, but the small study had limited power to detect a significant difference. However, while the relative efficacy of the two methods remains undefined, it is doubtful that continuous dosing of terbinafine will prove to be so much more effective than pulse dosing as to justify paying twice as much for the treatment of onychomycosis.

Continuous itraconazole (Sporanox®; Janssen) appears to be less efficacious for onychomycosis than continuous terbinafine and is more costly. Itraconazole is also associated with more drug-drug interactions than terbinafine. There is an FDA-approved pulse regimen of itraconazole (listed in package labeling for fingernail onychomycosis only).

Griseofulvin is not a cost-effective alternative for onychomycosis. Griseofulvin is fungistatic rather than fungicidal; the required duration of therapy is typically 12-18 months or more. Even with prolonged therapy, griseofulvin is only 15-30% efficacious for toenail onychomycosis and the relapse rate is estimated to be as high as 40%.

The most important factor to determine appropriate prescribing of terbinafine is *firm diagnosis of a fungal infection* when the nail-plate is sampled. Potassium hydroxide (KOH) prep, mycological culture, or PAS stain on histology are acceptable methods of confirming the presence of fungus on the nail-plate. If fungus cannot be documented, the diagnosis of onychomycosis should be re-evaluated.

In conclusion: Given DoD costs, terbinafine is more cost-effective than itraconazole for onychomycosis. Pulse dosing with terbinafine appears to be a reasonable alternative to continuous dosing and would decrease drug costs. Key issues in the treatment of onychomycosis include confirming that a fungal infection is present, and allowing sufficient time (3-6 months) after a course of treatment to allow the nail to grow out before considering retreatment.

Drug	Regimen	Pulse vs. continuous	Cost per regimen*	% of patients with mycological cure**
Terbinafine	250 mg po BID (for 1 week / mo x 3 mo)	Pulse	$ 158.34	80%***
Itraconazole	200 mg po BID (for 1 week / mo x 3 mo)	Pulse	$ 293.16	75-77%
Terbinafine	250 mg po QD x 12 weeks	Continuous	$ 339.30	73-94% (mean 77%)
Itraconazole	200 mg po QD x 12 weeks	Continuous	$ 628.20	63-67%

*DAPA prices as of 10/1/99; **Toenail onychomycosis; efficacy rates are derived from trials involving different patient populations and may not be strictly comparable; ***Based on a single trial (Tosti et al, 1996)

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Contract Updates

Concomitant Therapy with Cerivastatin (Baycol) and Gemfibrozil (Lopid, others) Contraindicated

- As a result of recent reports of rhabdomyolysis associated with concomitant use of cerivastatin and gemfibrozil, the Bayer Corporation has voluntarily changed the labeling for cerivastatin to state that the use of cerivastatin and gemfibrozil together is *contraindicated*. Patients who require concomitant use of gemfibrozil and an HMG-CoA reductase inhibitor (statin) should not be started on or switched to cerivastatin.
- All statins have labeling stating that the risk of myopathy and or rhabdomyolysis during treatment with statins has been reported to be increased with concurrent administration of fibric acid derivatives. Labeling for all statins also cautions that the combined use of a statin and a fibric acid derivative should be avoided unless the benefit of further alterations in lipid levels is likely to outweigh the increased risk of the drug combination.
- The DoD statin contract allows for non-contracted statins to be provided to individual patients in instances of medical necessity. If a patient requires concomitant therapy with gemfibrozil and a statin, it can be considered a medical necessity to use a non-contracted statin.
- FY99 prescription data from a sample of 21 MTFs suggests that about 3% of patients currently receiving any statin are receiving concomitant gemfibrozil therapy (see table below). The prevalence of this combination might vary considerably among MTFs depending on the local prescribing patterns and the scope and complexity of medical services provided.
- Please ensure that MTF prescribers and pharmacy personnel are informed of the labeling change for cerivastatin. Bayer and SmithKline Beecham field-based personnel have been informed of the labeling change and have been instructed to communicate this to prescribers and pharmacists. Questions concerning this matter should be directed to LCDR Mark Richerson at the PEC: (210) 295-9045 or DSN 421-9045 or by email at mark.richerson@amedd.army.mil.

Concurrent Use of Gemfibrozil and Statins: FY99 Prescription Data (sample of 21 Military Treatment Facilities)

	Q1	Q2	Q3	Q4	Mean
Patients on statins	27,754	29,336	30,830	31,441	29,840
Patients on statin + gemfibrozil	830	845	863	899	860
% of patients on combined therapy	3.0%	2.9%	2.8%	2.9%	2.9%

New Contract Awarded for Verapamil Sustained-Action Tablets

The DoD/VA contract for verapamil SA tablets previously awarded to G.D. Searle was terminated 12/1/99 due to the company's statement that it made a mistake on the price of the 240 mg 500-count bottle. A settlement has been worked out between contracting officials and G.D. Searle with regard to purchases of the 240 mg 500s during the effective dates of the contract (8/20/99-12/1/99).

A new award has been made to Zenith Goldline, with a base contract performance period of 12/1/99-11/30/00. Contract prices are given below. The contract does not include the 240 mg 30- and 90-count bottles.

This is a mandatory source contract for all DoD and VA facilities.

Contract Prices for Verapamil SA Tablets (Zenith-Goldline)

NDC	Strength	Count	Price/bottle	Price/tablet
00172-4285-60	120 mg	100s	$12.99	0.1299
00172-4286-60	180 mg	100s	$5.97	0.0597
00172-4280-60	240 mg	100s	$ 5.97	0.0597
00172-4280-70	240 mg	500s	$29.00	0.058

PEC POC: MAJ Don De Groff, MSC, USA
(210) 295-9635, DSN 421-9635
donald.degroff@amedd.army.mil